Development and Application of Versatile, Automated, Microfluidic Cell Culture System

Grant Award Details

Development and Application of Versatile, Automated, Microfluidic Cell Culture System

Grant Type: Tools and Technologies II

Grant Number: RT2-02052

Project Objective: development of an microfluidic tool to enable rapid and flexible screening of culture conditions to alter stem cell fates (differentiation, induction, direct reprogramming, maturation).

Investigator:

Name:	Marc Unger
Institution:	Fluidigm Corporation
Type:	PI

Human Stem Cell Use: iPS Cell

Award Value: $1,939,236

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Development and Application of Versatile, Automated, Microfluidic Cell Culture System

Public Abstract:

Supported in part by a previous CIRM Tools and Technologies Grant [REDACTED], we have optimized and scaled up highly advanced (microfluidic) cell culture chips into manufacturable form, produced prototype instruments to drive these chips, and demonstrated that we can culture cells, dose them with combinations of reagents, and export them back off the chip.

Since a cell's state is controlled by multiple genes, experiments to control cell state (e.g. to turn skin cells into stem cells, or to turn stem cells into nerve cells) will almost always involve multiple factors as well. We believe the ability to do multi-factor experiments more quickly, easily, and reproducibly will be enabling for the stem cell field.

The research we propose here will push the capabilities of this system even further by producing a set of three complementary commercial instruments: a Controller (capable of full fluidic and environmental control on one chip), a Hotel (capable of limited fluidic and environmental control on multiple chips), and a Reader (capable of imaging the cells in the chip in phase contrast and fluorescence modes). The idea is to load cells and dose them with different drugs/chemicals on the Controller, transfer them to the Hotel for culture and maintenance, and transfer them to the Reader for periodic imaging, allowing therefore running multiple sets of experiments in parallel and increasing even more the throughput of the system.

We are also proposing two sets of experiments to demonstrate what the system can do: in the first one, we will develop new methods to turn IPS cells (stem cells obtained by reprogramming non-stem cells - skin cells for instance) into neural progenitor cells – cells which can become different types of neural cells. These cells could be used to study diseases such as Parkinson's or Alzheimer's. In the second set of experiments, we will develop methods to make these cells proliferate without turning into specific types of neural cells. Since these types of cells are potentially useful to treat neurodegenerative diseases (e.g. Parkinson's and Alzheimer's) and spinal cord injury, developing methods to make more of them could advance the field a step closer to clinical application. In both cases, we will avoid using serum and animal products, since methods which use these products cannot be used clinically.

Statement of Benefit to California:

The research proposed here will allow bringing to the broad stem cell community, in and out of California, a commercial system that will accelerate research aiming at

1.) Identifying genes and small molecules affecting stem cell self-renewal and differentiation
2.) Identifying stem cell differentiation and expansion conditions

Since the grant will support work done in [REDACTED] and [REDACTED], and the end result will be the creation of a set of commercial instruments, there is a direct economic multiplier effect for the resources invested. In particular, at least three positions will be created (2 engineer positions and one postdoctoral position) as soon as the project starts.

The availability of the system will accelerate discovery of cell differentiation and expansion conditions, multiplying the power of stem cell research, in which California is a leader. The more efficient identification of differentiation and expansion conditions should enable new therapies. More directly, the discovery of conditions for differentiation of IPS cells into neural progenitor cells should enable the use of those cells as disease models (e.g. for Alzheimer's or Parkinson's); the discovery of chemically-defined conditions for expansion of those neural progenitor cells could lead to cellular therapies for neurodegenerative diseases like Alzheimer's or Parkinson's or spinal cord injury.

The availability of powerful tools in California, such as those we will develop here, will help ensure that these new therapies are pioneered in California, leading both to job creation and the availability of the most advanced medical care in the world for California citizens.

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